

OVERVIEW: When responding to these questions include the following in your discussion:

- Describe the circumstances and rationale for your comments.
- Provide examples with appropriate details (the complexity and context of the example should be provided).

QUESTIONS:

1. How can the clinical relevance of functional biological characterization studies (e.g., animal, cellular, binding assay) be established?
 - Under what circumstances can biological characterization studies be predictive of efficacy in humans and can this be used to justify limited clinical efficacy studies?
2. What are the appropriate standard(s) for the comparison of biological activities?
3. Based on biological characteristics, how can product-related impurities be distinguished from product-related substances and from the desired product? If a product-related substance can be identified/ distinguished, should the acceptance criteria be different for the follow-on product than that observed for the reference product?